A CONTRIBUTION TO THE STUDY OF ACUTE ASCENDING (LANDRY'S) PARALYSIS, WITH EXHIBITION OF SPECIMENS STAINED BY NISSL METHOD.

Dr. PEARCE BAILEY said, that the labor of preparing this paper had been equally shared by Dr. James Ewing and himself. Although it was nearly forty years since Landry described the disease which bore his name, there were to-day conflicting views regarding its pathology. The symptoms of the original case had been, acute paralysis ascending from the legs and arms, unaccompanied by marked loss of sensation, or by involvement of the sphincters. The intellectual faculties remained unimpaired. After death, no lesions were found in the nervous system to explain these symptoms, and careful microscopical examination of the the spinal cord by several observers was absolutely negative. The nerves were not examined.

The authors of this paper said that they had recently seen a case of acute ascending paralysis with extensive lesion in the spinal cord. The patient, a female, thirty-six years of age, was admitted to the Roosevelt Hospital, November 25, 1895, to the service of Dr. Francis Delafield. The family history was negative. The patient had previously enjoyed good health. On November 19, the disease began with vomiting, which continued until the third day, when she went to bed exhausted. She then began to have occasional attacks of vertigo, and dimness of vision. On November 23, she suddenly lost the power of both legs, and the next day there was paralysis of both arms. Sensation was undisturbed. The temperature was 101.4° at the time of her admission, and the urine examination was negative except for finding a few hyaline casts. The only important point in her personal history was that she had been a rather excessive beer-drinker. There was moderate ptosis on the left side; tactile sensibility was normal; there was no pain or tenderness in arms and legs; the bladder control was normal; the knee-jerks were lost; there was diminished response of the paralyzed muscles to the faradic current. On the 27th, she complained of headache and dyspnoea;

on the 29th, the urine contained a trace of albumen, and on the 30th, after a severe attack of pulmonary œdema, she died. At the autopsy, which was made twenty hours after death, the serous cavities were normal; the lungs were moderately congested; the bronchial lymph nodes were normal. The muscle of the heart was rather pale, and there were a few atheromatous patches in the aorta. The liver was reduced in size, and the general outline of the lobules was indistinct. The spleen was large and rather firm; its trabeculæ were faintly visible, and the Malpighian bodies imperceptible. The kidneys gave evidence of acute degeneration. Examination of the brain showed considerable distension of the veins and sinuses; there were no thrombi. Sections disclosed a large, but not distinctly abnormal blood-content. The consistence of the spinal cord was normal; the white matter appeared normal; the gray matter was plainly outlined and very slightly congested. The anatomical diagnosis was congestion and œdema of the lungs, acute degeneration of the kidneys, acute hyperplastic splenitis.

In the microscopical examination the Nissl stain furnished the most satisfactory result of the many stains tried. It is excellent for studying the changes in the ganglion cells; The vessels of the cauda equina were filled with blood; the axis cylinders of the nerve fibres appeared to be normal. The nerve fibres in the nerve roots appeared to be normal; in some nerve roots there was a slight perivascular infiltration of small round cells. Examination of the spinal cord showed the gray matter to be extensively affected throughout the entire length of the cord; there was intense congestion of all the blood-vessels, especially of the anterior branches of the spinal artery. Nearly all the vessels showed pronounced perivascular infiltration of small round cells. There was a diffused cellular infiltration of the gray matter, at times extending slightly into the white matter. The central canal appeared not to be especially affected. There was a more or less complete absence of chromophyllic masses in the cells. In some cells the cytoplasm was entirely bereft of chromophyllic bodies, being replaced by fine bluish particles. In the areas where the exudative inflammation was most pronounced, many shrunken cell bodies without visible cell nuclei were recognized with difficulty. In the white matter, where the inflammatory process extended into it from the gray matter, there was moderate perivascular infiltration. In the cortical region of the cord the lesions were most pronounced, while in the sacral region they were the least, many ganglion cells in the anterior horns remaining fairly well preserved. The lesions in the medulla and pons were chiefly marked in the gray matter, and were similar to those described in the cord. The nuclei of the cranial nerves were all more or less damaged, but chiefly in the sixth or seventh nerves. The basal ganglia showed the perivascular lesion and numerous small foci of cellular infiltration. The tempero-sphenoidal lobes were normal. Throughout the cerebellar cortex were found lesions similar to those found in the spinal cord. In the case just reported, the clinical symptoms were attributable to most extensive lesions affecting chiefly the gray matter of the spinal cord. The fact that the lesions were but slight in the sacral region explained the persistence of sphincter control.

There were many recorded cases, the speaker said, in which an ascending paralysis, unaccompanied by sensory symptoms soon involved the bulbar nuclei. An ascending paralysis pursuing a rapidly fatal course, without pronounced sensory symptoms, was a distinct clinical entity. These had always been considered the essential symptoms of Landry's paralysis.

To this paper was appended a table of all the carefully recorded cases, except those published in the Russian and Scandinavian languages, and a few old monographs. Several cases had been included which had been hitherto described as acute poliomyelitis anterior.

Fatal acute ascending paralysis might be divided into the following groups: (1) Cases in which no histological changes could be demonstrated in the nervous system; (2) those in which there was an acute exudative inflammation of the cord, medulla, and sometimes of the brain; (3) acute inflammation of the peripheral nerves; (4) acute inflammation, both of the central and peripheral nervous systems. In sixteen of the collected cases there were lesions limited to the cerebro spinal axis. A consideration of the etiology, symptoms and pathology of the disease point to the action of a toxic agent as the direct cause of the lesions. The lesions indicated an acute exudative inflammation, such as is usually found in cases having a bacterial origin. The authors had found it impossible to differentiate those various groups by their clinical manifestations. Their conclusions were: (1) That acute ascending paralysis was probably a toxæmia in which the poisonous agent affected chiefly the nervous system; (2) That its most common seat was in the spinal cord or medulla, though it might be present in the cortex and nerve roots; (3) That the lesions in other parts of the cerebro-spinal axis were of a similar nature; and (4) That when the lesion affected the peripheral nerves there was an increase in neuroglia cells.

Dr. BEVERLEY ROBINSON said that he had not seen more than one case of this disease, and that one had been reported some time ago to the Practitioner's Society. In the clinical history of that case there was no evidence of any toxæmia. The pathologist having charge of the case had failed to examine the nervous system by the improved methods detailed in the paper, or by bacteriological methods, but he had reported that there was little or no evidence of lesion in the spinal cord, although there were some pathological changes in the nerves themselves. The case had run a rapid clinical course, and the patient had died of œdema of the lungs.

Dr. C. L. DANA said that as he recalled Dr. Robinson's case, the clinical history was clearly one of Landry's paralysis, but there were no careful microscopical or bacteriological examinations reported; hence, though the case was apparently some form of toxic neuritis, there was no proof that the nerve cells were not primarily implicated. Three years ago, when discussing the subject with Mr. Victor Horseley, the opinion had been expressed that paralytic rabies might be classified clinically as Landry's paralysis, and that probably some of these cases were really examples of rabies. The sections at present under the microscope showed some cellular changes, yet the general pathological picture was that of a very marked vascular trouble—an infection or toxæmia. He would say most certainly that the primary changes were vascular, and those in the ganglion cells were secondary.

His experience with the Nissl stain had led him to place much less confidence in its revelations than did many others. In almost any brain, one could find all sorts of changes in the chromophyllic substance, and the method of preparing the staining and sections made it seem to him that it was almost impossible that there should not be considerable differences in the way in which the various cells took up the coloring substance.

The cortex cells in this specimen seemed nearly normal, although there was here evidence of this same vascular irritation. He thought that if the nerves had been examined it would have been found that they had been damaged even more than the nervous system. He recalled a case resembling Landry's paralysis, although running a slower course, in which there had been evidence of nervous and vascular irritation; the history of the case showed it to be rapidly fatal alcoholic neuritis.

Dr. B. SACHS said that Landry's paralysis had been buffeted about a great deal by various writers. Fortunately the day had passed when diseases were classified entirely on mere topographical lines. That there was a toxic agent causing Landry's paralysis he thought there could be no doubt, and, hence, it was to be particularly regretted that a bacteriological examination had been omitted in this, and many other cases. Since the bacilli of influenza had been found in cases of spinal cord troubles following that disease, it became incumbent on every careful observer to make a bacteriological examination in other acute infectious spinal troubles. He also felt that we should be very careful in making inferences regarding slight changes in the structure of the cells in specimens stained by Nissl's method. In the case reported in the paper, one of the chief symptoms had been absence of sensory disturbance quite early in the disease. If this one clinical feature must be accepted as essential, we could not suppose that the changes which had been described were those chiefly responsible for Landry's paralysis. It was more than probable that the changes occurred not only in the brain, but in the spinal cord, and the peripheral nerves.

Dr. GEORGE W. JACOBY said that if we accepted Landry's definition of the paralysis, we could only make a clinical diagnosis, for Landry claimed that there must be a lack of anatomical evidence. He had been struck by the fact that in the case described in the paper the patient was a beer-drinker, and that the symptoms had developed quite rapidly. This had been noted in quite a number of cases. The lesion might be localized in the cells of the spinal cord or in the cortex. The report presented seemed to indicate that in the future we would probably find pathological changes in the cell body analogous to those which had been thus far found in the peripheral nerves. It would seem that we were dealing with a chronic alcoholic intoxication of the central nervous system.

Dr. LANDON CARTER GRAY said he thought that the paper just presented was an extremely valuable contribution to the subject of Landry's paralysis. He could recall a number of cases of this disease, which could be divided into several groups. Some of these had rapidly proved fatal; some had run a slower course; some had improved and then relapsed. Those, which had recovered, had subsequently had atrophy of the muscles, and had presented a condition similar to that of poliomyelitis. He had also seen cases of alcoholic neuritis presenting several types—some few had died, some had had obstinate vomiting for days and weeks, some had passed into a miserable condition of invalidism. He could not recall any of these cases having recovered. The clinical definition of the disease could not be taken as anything more than a guide. Undoubtedly there was an underlying toxæmia, and possibly an infection. It seemed to be pretty generally agreed that Nissl's stain was still on trial, and certainly some very serious objections had been made to it, so that our deductions based upon it must be made with great caution.

Dr. JOSEPH COLLINS said that the paper just contributed had served to crystallise what had been in our minds, *i. e.*, that Landry's paralysis had been handicapped by a name and a tradition, which for years had prevented us from forming a legitimate conception of the pathology of the disease. All must have been impressed with the fact that Landry's paralysis was a disease dependent upon a poison, and that its clinical forms varied as to the part of the nervous system implicated. It had not yet been proven that the disease was one of the spinal cord or of the peripheral nervous system. When it had been said that Landry's paralysis was a disease dependent upon infection, or upon a toxic substance manifesting its action on a well defined part, or on the entire nervous system, the pathological location of the disease, so far as known, had been stated. In the case reported in the paper the lesions were universal, hemorrhagic splenitis, parenchymatous nephritis and an exudative inflammation in the spinal cord, all of which pointed to an infection. The changes in the cord were virtually those of acute anterior poliomyelitis, a disease which was very probably due to some micro-organisms. The underlying condition should not be described as a "toxæmia," which meant a primary blood infection, but as toxic. If epidemic cerebro-spinal meningitis and acute anterior poliomyelitis had been shown in a number of instances to have been associated with pyogenic micro-organisms, why should not Landry's paralysis be dependent upon such a condition also?

Dr. SACHS said that in almost every case in which the disease had been named after the person, who had first described it, an unusual reverence had been shown for the symptomatology first reported. Thus, Landry had insisted that there should be bulbar complication, yet this was more or less accidental, although present in most of the cases. It would not be right, it seemed to him, to exclude all those cases in which the process had not extended into the medulla, provided the other symptoms were those of acute ascending paralysis. It would be better to speak of the disease under discussion as Acute Infectious Ascending Paralysis.

The PRESIDENT said that it seemed to him that the so-called Landry's paralysiswas an acute infectious process, which at times affected the spinal cord, and at other times affected the nerves to a greater extent. He could not see how it at all resembled the ordinary cases of even the most acute alcoholic multiple neuritis.

Dr. JAMES EWING thought the Nissl stain had been very generally accepted as the best method of studying the pathological changes in the ganglion cells. Dr. Dana's trouble with this stain was probably due to the use of alcohol as a hardening agent; the cells should be treated with bichloride of mercury. The examination of the cauda equina and the nerve roots in this case seemed to absolutely negative the opinion expressed by Dr. Dana, that in the nerves, if examined, would have been found even more pronounced changes. We would have to assume that the central nervous system and the peripheral nerves were markedly affected, and yet the intervening portion, the nerve roots, had escaped. In the case reported, sensory symptoms were almost entirely absent. A careful examination of the literature showed that cases of acute multiple neuritis resembling Landry's paralysis were exceedingly rare. The word "toxæmia" had been used advisedly in the paper, for the authors were not ready to state that Landry's paralysis was an acute infectious disease. They used the word "toxæmia," because they believed the disease was produced by a toxic agent in the blood, which, at least in some cases, was of a bacterial nature.